ORIGINAL ARTICLE

Development of a Malaysian Web-based Application to Support Caregivers of Children with Amino Acid Metabolism Disorders (AAMDs)

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ABSTRACT

Background: Individualised dietary intervention is paramount in the treatment of amino acid metabolism disorders (AAMDs). However, dietary monitoring was perceived as tedious as it required minute weighting of the food items and a complex calculation process. The present study aims to elaborate on the development and content validation of MyProteinGuide™, a web-based application among caregivers of children with AAMDs. **Methods:** The overall content of the MyProteinGuide™ was shaped by the results obtained during a needs assessment and supported by an evidence-based approach which consists of self-monitoring features and informative educational content. Content validation was then carried out among nine healthcare professionals. **Results:** The overall CVI of the module was 0.983, which was deemed validated for content. Suggestions for improvements to MyProteinGuide™ in terms of content features included having a wide variety of menu and recipes, using different household measurements as units in food diary and a specifically labelled growth chart. In terms of language and GUI, using a uniform colour scheme and standardisation of language was suggested. **Conclusion:** Improvements to the application according to healthcare experts' comments should be addressed to optimize the usage of MyProteinGuide™ among caregivers of children with AAMDs.

INTRODUCTION

Amino acid metabolism disorders (AAMDs) manifest through a deficiency in functional enzymes or transporters, resulting in the accumulation of normal or unusual compounds such as amino acids, ammonia, and organic acids in proximity to the metabolic impediment. AAMDs can be further classified into three subgroups such as urea cycle disorders (UCD), organic acidurias (OA) and aminoacidopathies (AA) (Ferreira et al. 2021). Among all subclasses of AAMDs, AA such as Maple Syrup Urine Disease (MSUD) and Phenylketonuria (PKU) was the most prevalent disorders in Malaysia (Lim et al., 2023). This accumulation can cause acute or progressive intoxication (Ezgu, 2016; Saudubray et al., 2016). In the management of AAMDs, a lifelong, personalized protein-restricted diet holds crucial significance. This diet serves to reduce the production and deposit of toxic metabolites as well as to prevent catabolism by providing adequate macronutrients (Frazier et al., 2014; Jurecki et al., 2019; van Wegberg et al., 2017)

This diet demands a high degree of adherence on the part of all family members which significantly affects the quality of life (QoL) of both the patients and their caregivers (Bosch et al., 2015; Eminoglu et al., 2013; Fabre et al., 2013; Shaji Thomas et al., 2021). This is evident in the daily food preparation process, which includes meticulous weighing and calculations for accurate natural protein intake, which are viewed as time-consuming (Fabre et al., 2013). Besides the tedious calculation process, caregivers are tasked with preparing the daily menus for their children, often involving extra cooking due to the children's inability to consume the regular family diet (Eijgelshoven et al., 2013). Simultaneously, there is a need to adjust the natural protein intake over time, given its customization based on individual factors such as the severity of the condition (including residual enzyme

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activity), age, growth rate, and metabolic control (MacDonald et al., 2012). In addition to that, caregivers need to possess comprehensive knowledge regarding the preparation of their children's daily diet, incorporating a wide variety of low-protein ingredients to prevent monotony in their meals (Lim et al., 2022).

With rapid integration of digital health monitoring for the improvement of quality of life, it was found that diet tracking mobile applications can ease the monitoring of patients' daily nutrient intake. These applications auto-calculate the energy and macronutrients of every food item entered, and then compare the results to the patient's individual requirements determined by their dietitian (Ho et al., 2020). Hence, similar concept was proposed among patients with AAMDs (Ho et al., 2016). Dietitians may require less time analyzing diet recall during diet consultations, freeing up more time spent in providing nutrition education. The dietary application's ability to provide instant analysis of children's daily natural protein intake can motivate caregivers to track their children's protein intake for longer periods, thus promoting self-monitoring and sense of self-efficacy.

A plethora of mobile and web-based applications specifically for patients with AAMDs is now available in mobile app stores and on web pages. Their roles as dietary self-management tools for patients with AAMDs can be used in a variety of ways, including as protein and specific amino acid trackers, food diaries, digital food composition databases, and nutrition recommendation providers (Ho et al., 2016). In terms of content, Lim and colleagues assessed six mobile applications that are commercially available and designed for people with metabolic disorders, and found several limitations (*unpublished data*). Firstly, the food composition database in most self-management systems available in the market is not culturally appropriate for use in Malaysia. This is because these systems were developed in Western countries, such as Germany and Canada, and may not suit the dietary habits of the local Malaysian population due to differences in language, culture, and health behaviour. Besides that, the basic educational materials are mostly not adopted from credible clinical guidelines. The educational materials are also often too lengthy, and do not use graphics to describe the pathophysiology of disorders. Instead, they only focus on delivering the nutritional content of food and monitoring the dietary intake of the patient (Ho et al., 2016). Furthermore, the systems lack anthropometric and biochemical monitoring, as well as elements of nutritional education such as low protein recipes. Importantly, none of these applications have been validated by healthcare professionals with experience in managing metabolic disorders. To date, neither a web-based nor a mobile application has been developed specifically for patients with AAMDs in Malaysia. Hence, this study aimed to develop and evaluate a web-based application specifically for patients with AAMDs in Malaysia, using the Malaysian food composition database as a reference.

MATERIALS AND METHODS

This study consisted of three phases. In Phase 1, a needs assessment was conducted using a mixed-methods approach. This involved organizing focus group discussions (FGD) and questionnaire surveys with caregivers of patients with AAMDs were conducted (Lim et al., 2023). Phase 2 involved developing and validating the MyProteinGuide™ among healthcare professionals, including dietitians and clinical geneticists, while Phase 3 commenced a cross-sectional study to evaluate the usability of the web-based application among caregivers (not reported in this manuscript).

System development

MyProteinGuide™ was developed using the IDEAS framework (Integrate, Design, Assess and Share), which was developed by Mummah and colleagues (Mummah et al., 2016) to create digital health behaviour change interventions. The IDEAS framework proposes a four-step approach, including integrating the needs of the caregivers of patients with AAMDs, which were identified through the FGDs and qualitative survey (Lim et al., 2023), followed by designing the contents iteratively and rapidly together with group of experts consisting of lecturers from the dietetic programme, a clinical psychologist, a metabolic dietitian and a consultant clinical geneticist. After that, assessment of the application was carried out via usability testing among the caregivers. Sharing was carried out via the publication of this article. The interface for signing up for a new account is shown in Figure 1. The overall description and content features of the MyProteinGuide™ are described in the section below.

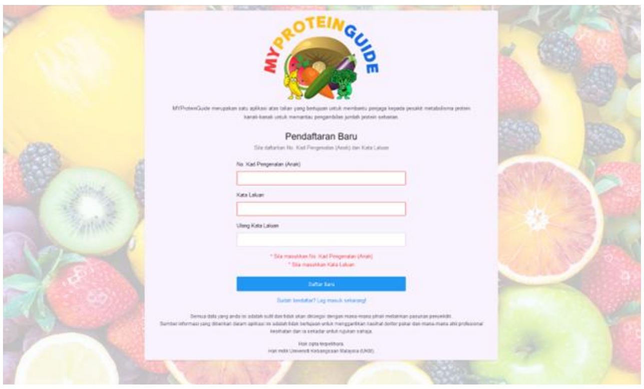

Figure 1: Interface signing up a new account

Personal profile

Once users create an account, they can enter the child's sociodemographic profile, such as birthdate, gender, and race (Figure 2). Furthermore, the caregivers need to fill in their child's energy, total protein, and total natural protein requirement based on the prescription given by their clinical geneticist and metabolic dietitian during each clinic appointment. The total energy requirement for children with AAMDs is usually determined by the metabolic dietitian based on the child's age and gender, according to the Malaysian Recommended Nutrient Intake (RNI) 2017 (Ministry of Health Malaysia, 2017), as the energy requirement of AAMDs children is similar to that of normal children (Dixon et al., 2014; Frazier et al., 2014; Jurecki et al., 2019).

Besides that, the total protein requirement of all patients with AAMDs except those with urea cycle disorders (UCD) will also be determined based on the Malaysian RNI 2017, with an additional 20-40% of the total protein for patients who consume synthetic metabolic formula (Frazier et al., 2014).

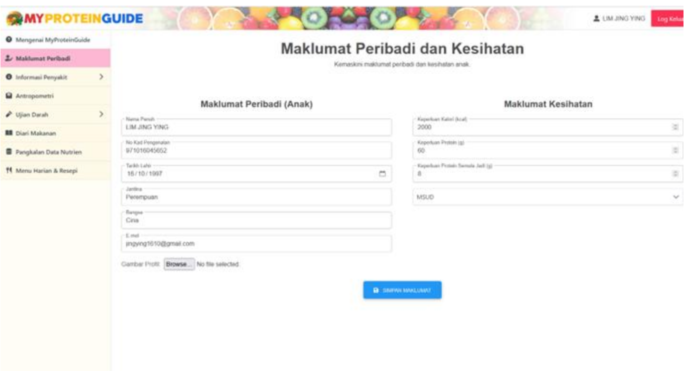

Figure 2: Personal profiles of the patients with AAMDs

Disease information

This section introduces all 10 AAMDs (Figure 3). This comprises basic information about each disorder, such as the underlying pathophysiology of the disrupted metabolic pathway, clinical signs and symptoms, and the medical nutrition therapy (MNT) for the specific AAMD.

All the information is presented in infographics for easy comprehension. The evidence-based practice for the diagnosis, evaluation, prevention, and treatment of inherited metabolic disorders is provided, as outlined in the clinical dietetics for paediatrics guideline (Dixon et al., 2014). All the information has been verified by clinical geneticists on the research team.

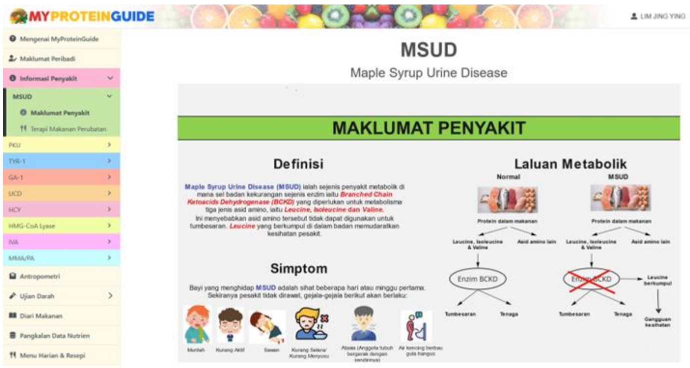

Figure 3: Diseases Information

Anthropometric measurement

This feature aims to streamline and standardise weight monitoring and growth tracking of patients with AAMDs (Figure 4). Caregivers can enter the values of body weight and height at each appointment in the genetic clinic. The interpretation of the BMI will be based on the shaded colour of the graph.

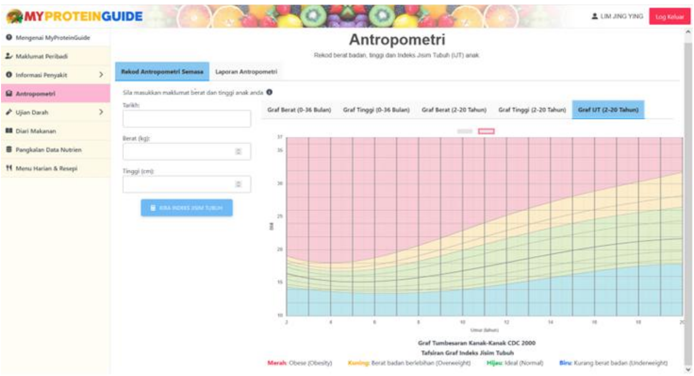

Figure 4: Anthropometric Monitoring

The 2000 Centre for Disease Control and Prevention (CDC) growth chart was used as the reference growth chart as it describes the growth of children in the United States from birth to 19 years of age. The CDC classification of growth indicators is shown in Table 1.

Table 1: Interpretation of CDC Growth Chart

BMI Percentile	Interpretation
< 5th percentile	Underweight
5th – < 85th percentile	Normal
> 85th and < 95th Percentile	At risk of overweight
> 95th percentile	Overweight

Biochemical data monitoring

This feature allows users to record their children's plasma amino acids levels in the application after each genetic clinic appointment (Figure 5). All the biochemical parameter values entered will be plotted into a graph to show the trend over time. The maximum and minimum reference ranges for plasma amino acids will be labelled in colour on the graph.

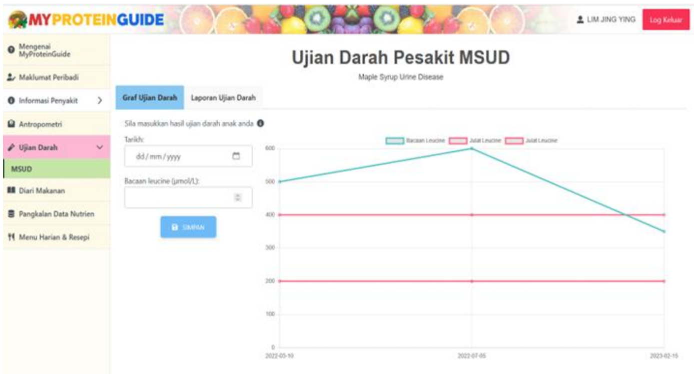

Figure 5: Biochemical Monitoring

The parameters and their reference ranges used to monitor patients with inherited metabolic disorders were determined based on clinical guidelines that have been published previously. The research team consulted with clinical geneticists and metabolic dietitians to further verify the findings. The parameter(s) used to monitor the metabolic control differ depending on the particular AAMD, as each disorder is caused by a different single enzyme deficiency that blocks a specific metabolic pathway. The specific plasma amino acids for each disorder are listed in Table 2.

Table 2: Specific plasma amino acid for monitoring

Types of AAMDs	Plasma amino acid
Maple syrup urine disease (MSUD)	Leucine
Phenylketonuria (PKU)	Phenylalanine
Tyrosinemia (TYR)	Tyrosine
Urea cycle disorders	Ammonia Glutamine Arginine
Glutaric Aciduria Type-1 (GA-1)	Lysine
Propionic Aciduria (PA)/ Methylmalonic Aciduria (MMA)	Ammonia
Isovaleric Aciduria	Isoleucine
HMG CoA Lyase	Leucine Ammonia
Homocystinuria	Homocysteine

Digital food composition database

The digital food composition database consists of 17 food groups (Figure 6). Our database excludes meat and meat products, eggs, fish and shellfish, milk and milk products as all these food items are typically inhibited in the diet (Boyer et al., 2015). In addition to that, the food composition database consists of the nutrients content of all metabolic formulas and modular formulas. The calories and macronutrients content as well as the weight (gram) and serving size of the food items are all displayed.

Figure 6: Digital food composition database

Food diary

Caregivers can use the food diary to record their children's daily intake of food and drinks, with the weight of the raw food items in grams required to be entered in the system (Figure 7). The macronutrients of each food item entered will be calculated automatically using the weight of the raw food entered and linking each food item to the digital food composition database as described previously. A bar chart will be used to track the daily number of calories, total protein, and targeted natural protein intake. The targeted natural protein is calculated by subtracting the protein from the metabolic formula from the total protein. Users can also trace their food intake for the past 30 days, which can be shared as a report with their metabolic dietitian.

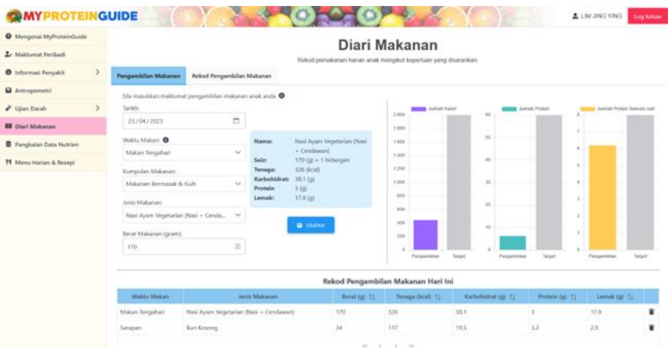

Figure 7: Food Diary

One-day Menu and Recipes

The MyProteinGuide^{TM} application also provides examples of one-day menus (Figure 8). These menus contain low protein foods and dishes for breakfast, lunch, and dinner which will make up a total of 5g, 8g, 10g and 12g of natural protein. These menus offer caregivers ideas about diet preparation for their children. Besides that, it also provides examples of low-protein recipes which were formulated and modified by dietitians on the research team (Figure 9). The process of recipe development was described in the next section.

Figure 8: Digital food composition database

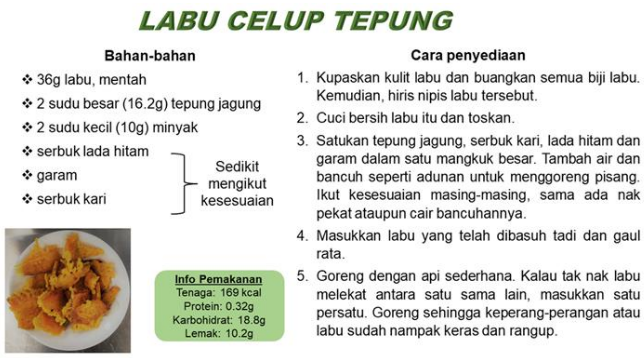

Figure 9: Example of Low Protein Recipes

Low Protein Recipes Development

After obtaining suitable recipes from recipe books or websites, the modification process was carried out by considering the individual's tolerated range of natural protein. The ingredients used in the recipe formulation were selected based on the following factors: the common low protein foods that patients consume, the amount of natural protein per serving, availability, price, cultural appropriateness, and the method of preparation.

With regard to the weaning diet recipes, they consist of 0.5-1.0g of protein per meal, while the main meal recipes consist of 2.0-3.0g for each meal. The main ingredients used in formulating low-protein recipes mostly consists of cereals, vegetables, and fruits. Snacks were modified using low protein flour and other flour products with minimal protein content, such as corn flour and tapioca flour, which are easily available and affordable. The nutritional values of all the recipes were calculated using the Nutritionist Pro™ software.

All the ingredients calculated were weighed accurately for cooking. A student researcher and other research enumerators weighed the ingredients accurately according to the calculations and then prepare and cooked the dishes in the diet therapeutic lab of the Faculty of Health Sciences, Universiti Kebangsaan Malaysia (UKM). Furthermore, three panels of clinical dietitians and academic dietitians or nutritionists who specialized in the paediatric field conducted sensory evaluation.

The recipes were evaluated for their colour, appearance, body and texture, taste and flavour and overall acceptability using a five-point hedonic scale, comprising: 1= dislike extremely, 2 = dislike moderately, 3 = neither like nor dislike, 4 = like moderately, and 5 = like extremely. A score of more than 3 indicated that the recipes were on average acceptable (Muhimbula et al., 2011). The process of recipe modification is simplified in Figure 10.

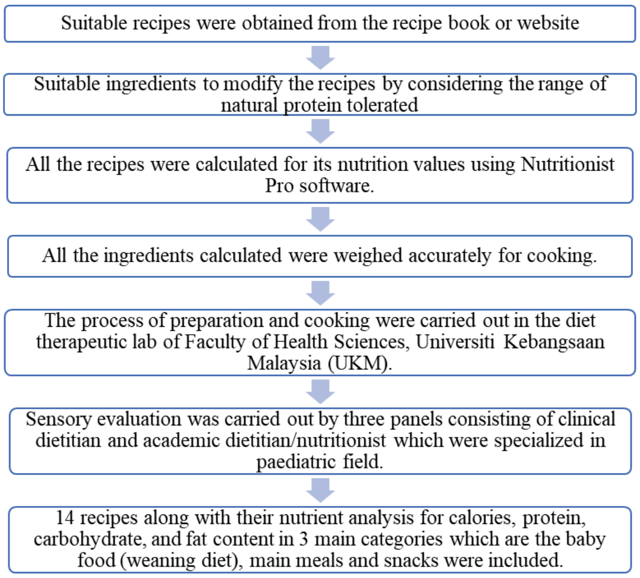

Figure 10: Flow chart illustrating the process of modifying recipes

Methodology for Validation Study

According to Yusoff (2019), the number of experts for content validation should be at least six and does not exceed 10. Hence, content validation was carried out among nine experts, including five dietitians with a minimum of one year of clinical experience in managing inherited metabolic disorders, and four consultant clinical geneticists. The evaluation considered the relevance, appropriateness, ease of use, accuracy of the language used in the features content, and attractiveness and appropriateness of the graphical user interface (GUI) based on the four-point scale (1 for "not relevant"; 2 for "some revision required"; 3 for "relevant but needs minor revision" and 4 for "very relevant"). Lastly, the content validation index (CVI) was calculated, which measures the proportion of items on the scale that achieve a relevance scale of 3 or 4 by all experts (Yusoff, 2019).

Ethical Approval

This study was approved by the Medical Research Ethics Committee (MREC) (NMRR ID-22-00762-UKN) and the Secretariat of Research Ethics Committee, Universiti Kebangsaan Malaysia (JEPUKM-615 2021-765).

RESULTS

Evaluation of low protein recipes

All the recipes provided in this website have scored a minimum of 3 out of 5 points in term of taste, appearance, smell, mouth feel, aftertaste and general acceptability indicating good acceptability (Table 3).

Table 3: Evaluation of Low Protein Recipes

	Taste	Appearance	Smell	Mouthfeel	After taste	General acceptability
Nasi Minyak + Kurma Kentang	4	4	4.3	4.7	4.3	4
Soo-Hoon Goreng	43	4.3	4.3	4.3	4.3	4.3
Laksa Goreng	3.7	3.7	4.3	4.3	4.3	4.3
Nasi Ayam Vegetarian + Cendawan Tiram Goreng	4.0	3.7	4.3	3.7	4.0	4.0
Nasi Tomato	3.0	4.0	3.7	3.0	3.0	3.0
Puding Sago Gula Melaka	5.0	5.0	4.7	5.0	5.0	5.0
Cucur Nasi	4.0	3.3	3.0	3.7	3.7	3.7
Agar-agar Laici	5.0	5.0	4.7	5.0	5.0	5.0
Labu Salut Tepung Jagung	4	4.5	4.5	4.0	4.5	4.0

Content Validation of the Module

The "Content features" of MyProteinGuide™, received a CVI of 0.982, which indicates that there was an excellent level of agreement between the experts on the content validity of the module as shown in Table 4. As the overall CVI of the module was 0.983, the module was deemed validated for content. Most experts (5/9; 56%) rated all the 6 features of MyProteinGuide™ as very relevant, while the remaining rated them as relevant but needing minor revision. Moreover, 77.8% (7/9) of experts rated the language used in MyProteinGuide™ as appropriate, easy to understand, and accurate. Lastly, 66.7% (6/9) viewed that the GUI was appropriate and attractive.

Table 4: Content validity index for MyProteinGuide™ by expert panel members (n=9)

Criteria	Item Description	I-CVI
Content Features	Disease Information	1
	Anthropometric Monitoring	1
	Biochemical Monitoring	1
	Food Diary	1
	Food Composition Database	1
	Low Protein Recipe & One-day Menu	0.889
Average CVI		0.982
Language	Appropriateness for users >18 years old	1
	Accurateness of the terms used	1
	Easiness to understand	1
Average CVI		1
Graphic User Interface (GUI)	Attractiveness of the colour scheme	0.889
	Appropriateness of the font size and easiness to read	1
	Appropriateness of the characters/ icon/logo	1
	Appropriateness of the layout (label, button, info) in each screen	1
Average CVI		0.972
Overall CVI		0.983

Overall, the healthcare professionals rated the module positively. They considered the module informative and relevant for monitoring the metabolic and health status of patients. Despite the positive feedback, some healthcare experts raised concerns regarding the content features, language used, and user interface. Table 5 summarized the suggestions made by expert panels to improve the MyProteinGuide™.

Table 5: Suggestions by expert panels to improve MyProteinGuide^{TM}

Main Topics	Descriptions
Content Features	- Standardisation of terms used in describing the metabolic pathway - Gender-labelled growth chart - Updated list of metabolic formulas and its nutrient contents - Include HBV protein food sources - Increase variety of recipes - Auto-tailored recipes for specific diseases - Include photos of food items with proper portion size in the food composition database - Inclusion of household measurements in quantifying portion size
Language	- Correction of spelling errors - Standardisation of language used
Graphic User Interface (GUI)	- Standardisation of colour picture

DISCUSSION

This study describes the development of the web-based application, MyProteinGuide™, which provides personalized content, including self-monitoring and educational features, to help caregivers of children with AAMDs effectively track their dietary habits. The key feature of this application is that it includes mostly all of the components of nutritional assessment, including client history, anthropometry, biochemical data, and dietary history monitoring, as outlined in the nutritional care process (Writing Group of the Nutrition Care Process/Standardised Language Committee, 2008). Compared to the traditional method of tracking weight changes, plasma amino acid values, and diet history in separate sheets manually, MyProteinGuide^{TM} is more convenient for both caregivers and healthcare professionals of patients with AAMDs to pinpoint certain foods, total natural protein intake or metabolic formula consumption that may be influencing patients' plasma amino acid readings (Chen et al., 2018). A previous study developed an application that helps patients with 15 different inborn errors of metabolisms (IEMs) track the amino acid content of foods that are specific and relevant to their IEM (Ho et al., 2016). For instance, patients with maple syrup urine disease (MSUD) can track the leucine content of foods. However, our study did not include the amino acid content in our application as it is the practice in our hospital to focus on total natural protein intake only, instead of amino acid contents. In addition to that, our study was not only focused on providing dietary monitoring, but also on creating an 'all-in-one' application that includes all the components of nutritional assessment to simplify the self-monitoring process.

To the best of author's knowledge, this is the first dietary self-monitoring web-based application that was designed specifically for caregivers of patients with AAMDs using a user-centred approach, involving discussions with users from the early stages of development. Considering the heterogeneous nature of AAMDs, it is essential to individualise and prioritize user needs to the specific needs and profiles of each caregiver to enable more appropriate web design and ensure effective outcomes (Gabrielli et al., 2017). One of the highlights of the MyProteinGuide^{TM} web-based application is the incorporation of individualised energy and total natural protein requirements with automated calculation of dietary intake progress using real-time data interpretation feature (Ahn et al., 2019). By reducing the burden of food preparation, this features provides more time and energy of caregivers, which can then be used to support the person with dietary self-management (Quesada-Lopez et al., 2016). Besides that, to accommodate the needs of diverse users and provide personalized content, the one-day menu included different amounts of protein and low-protein recipes suitable for different age groups. Unlike previous studies, which did not evaluate the specific recipes included in their application (Ramanathan et al., 2013; Salihah et al., 2017), our study conducted food sensory testing on the modified low-protein recipes among the healthcare providers to validate its suitability for patients with AAMDs. Interestingly, the food sensory test was not conducted with the actual patients with AAMDs due to practical and ethical considerations as most of the patients were aged below 12 years old. This approach had been used in preliminary recipe development in which thehealthcare professionals had tasted the end products to determine the acceptability of these modified recipes among the target population (Ettinger et al., 2014).

In addition, the features of MyProteinGuide^{TM} were specifically designedbased on data collected from the FGDs during the requirements analysis stage. In the context of our study, AAMDs are a group of chronic disease in which it is essential to adhere to a specific amount of natural protein in the diet to ensure the patients' plasma amino acids are maintained within a normal range that does not cause neurotoxicity. Adequate calorie intake is also important to prevent catabolism and maintain a normal body weight, which can improve and maintain quality of life (Boyer et al., 2015; Frazier et al., 2014). As such, all of the features in this application were designed to address the challenges that caregivers face when assessing the needs of patients with AAMDs (Lim et al., 2022), ultimately, leading to successful dietary treatment and adherence.

All the expert panels involved in this study agreed that the content validity index (CVI) of MyProteinGuide™ was rated as appropriate. The healthcare professionals also found many positive features about the application's components and functionalities. However, a deeper analysis of the healthcare experts' feedback on the content features of the MyProteinGuide™ indicated that providing additional support for defining food quantities using household measurements instead of using weight would ease the dietary monitoring process. Another suggestion for improving the application was to add high biological value (HBV) protein sources such as chicken, fish, egg and their products, however, this may be controversial among the healthcare providers. The allowance for natural protein varies among different types of AAMDs. Some patients with a higher allowance for natural protein are allowed take the HBV protein. To accommodate this discrepancy, more advanced settings should be included to enable users to customize the food database, menus, and recipes to their specific type of AAMDs. Nevertheless, this type of automatically generated tailored information to the existing application would require greater expert technological knowledge and skills, more time, and extensive financial resources (Simons et al., 2018).

The key strength of this study is the involvement of caregivers of patients with AAMDs and healthcare practitioners in the app development process, which allowed the app to be tailored to the needs and preferences of caregivers. The development of MyProteinGuide™ was a structured process that involved collecting qualitative data from caregivers of children with AAMDs in Malaysia. The modules were then developed based on this data, and the application was adapted to the specific needs of these Malaysian caregivers in several ways, such as using simple Malay language, providing ample white space for easy navigation, and tailoring the content to the cultural preferences of Malaysians by including a variety choice of recipes using local products and their nutrient analysis based on the Malaysian food composition database.

There are several limitations in this study. Firstly, some app features could not be implemented due to limited time and financial resources, even though they were of interest to the target group. These features included highly personalized advice tailored to the health status, in-app notifications as a reminder, and a social forum for caregivers to communicate with each other. Future versions of the app may need to include these features. Next, the choice to develop a web-based application instead of a mobile-friendly (responsive) version may limit its usability and for self-monitoring. In addition to that, MyProteinGuide™ is specifically adapted to the Malaysian population, which limits its generalizability to other populations. Hence, it is suggested to translate it into other languages and adapt the content, such as the ingredients used in the recipes, to make it more accessible to other target groups worldwide.

CONCLUSION

MyProteinGuide™ has the potential to become an effective solution for supporting self-monitoring of nutritional status and delivering nutrition education for caregivers with children with AAMDs. The user-centred design and evidence-based approach used to design the application which combines setting individualised energy and protein prescription, nutritional status monitoring and educational components such as low protein recipes, represents a significant advance over the functionality of current available commercial application for patients with AAMDs. Future refinements of the application should be taken into account and addressed accordingly to optimize its use among caregivers of patients with AAMDs.

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